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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,928	10/13/2006	Bruce Joseph Roser	TOPT0103PUSA	6692

28395 7590 03/03/2009

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EXAMINER	
HEYER, DENNIS	

ART UNIT	PAPER NUMBER
4121	

MAIL DATE	DELIVERY MODE
03/03/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,928	ROSER, BRUCE JOSEPH	
	Examiner	Art Unit	
	DENNIS HEYER	4121	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/04/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Status of Claims

Claims 1 – 11 are currently pending

Priority

This application, filed 10/13/2006 is a national stage entry of PCT/GB05/50050, international filing date 04/13/2005 and claims the benefit of foreign priority to GB0408199.8, filed 04/13/2004 and GB0504501.8, filed 03/07/2005. The Claims from the instant application are supported in the specification of foreign priority document GB0408199.8, filed 04/13/2004.

Claim rejections – 35 USC § 112 – 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 – 10 are rejected under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The parameters "m" and “n” in the general formulas for the fluorinated liquids are defined neither in Claim 1 nor in the specification which renders Claim 1 and all claims dependant from Claim 1 indefinite.

Claim rejections – 35 USC § 112 – 1st Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 -10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1st "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January *5,2001.*

Claim 1 is drawn to a formulation comprising liquids of the following general formula:

R1-X--R2 or

R1-X-(CF2Y)n(CF2CF2Z)m-R2 or

R1-[(X-CF-R2)n-(X-CF2)m]OR3

where X, Y and Z are defined as O (oxygen), an ether, NR3 (N=nitrogen), an amine or S (sulphur); and each of R1, R2 and R3 are defined as a non-fluorinated, partially fluorinated or fully fluorinated alkyl, cycloalkyl, aryl or arylalkyl group or an organic functional group, halogen group or cyano group.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain

species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus …") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the

claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to a formulation comprising liquids of the following general formula:

R1-X--R2 or

R1-X-(CF2Y)n(CF2CF2Z)m-R2 or

R1-[(X-CF-R2)n-(X-CF2)m]OR3

where X, Y and Z are defined as O (oxygen), an ether, NR3 (N=nitrogen), an amine or S (sulphur); and each of R1, R2 and R3 are defined as a non-fluorinated, partially fluorinated or fully fluorinated alkyl, cycloalkyl, aryl or arylalkyl group or an organic functional group, halogen group or cyano group.

As noted in the instant specification the prior art discloses formulations for stabilized suspensions of particles comprising a bioactive agent in a liquid such as a perfluorocarbon such as perfluorodecalin.

The specification discloses a single working example in which the liquid, a specie of Claim 1, is the hydrofluoroether HFE 7500 (page 6). The instant specification also discloses two structurally related species within the limitations of Claim 1, the hydrofluoroethers HFE 7200 and HFE 7100 (page 4). However, the genus of Claim 1

encompasses a broad range of structurally and functionally diverse species such as amines and thioethers which have physical and chemical properties distinct from fluoroethers.. For example, certain thioethers are subject to oxidation which alter their polarity, amines are basic and may react with acidic sites present in the active ingredient preserved in the glassy particles of Claim 1. Amines may also act as nucleophiles and chemically modify said active ingredients. The genus of Claim 1 also includes species containing "an organic functional group". Such groups can comprise an even more diverse range of structurally and functionally distinct compounds, including carboxylic acids, epoxides, unsaturated ketones etc. Some of these organic functional groups are well known to react with active ingredients, such as biomolecules, and modify their structure, leading to a change in biological properties. Finally, the general formula of instant Claim 1 comprises both small molecules and polymers. The range of polymer size is unclear as, the terms "m" and "n" are not defined (see 112 2nd paragraph rejection above). In any event, the physiochemical properties of such polymers and traditional small molecules are very different.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1 is broad and generic, with respect to all possible compounds encompassed by the claims. The possible structural variations of Claim 1 are almost limitless, encompassing any fluorine-containing ether, thioether or amine (X, Y and Z) and any organic functional group (R1, R2 and R3). Although the claims may recite some functional characteristics, the claims lack written description because there

is no disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. Moreover, the, as noted above, the specification lacks sufficient variety of species to reflect this variance in the genus. The disclosure, in the working example of the instant specification, of a stable suspension of particles, with little tendency to aggregate, in the small molecule hydrofluoroether solvent , HFE 7500 does not provide sufficient descriptive support for the myriad of compounds comprising diverse functional and structural properties embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 – 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roser, J.R. in US patent 6,190,701 (published: 02/20/2001) in view of Johnson, K.A. in US patent 5,376,359 (published: 12/27/1994) and Owens, J.G, in Low GWP Alternatives to HFCs and PFCs, Report of 3M Company Specialty Materials, St. Paul, MN, USA (2000).

Instant Claim 1 is drawn to a composition comprising an active ingredient preserved in a particle and suspended in a fluorinated solvent. As noted above, instant Claim 1 has already been rejected under 35 U.S.C. 112, second paragraph as being indefinite for failing to define the terms "m" and "n". The Roser reference teaches a composition comprising a bioactive compound and sugar glass particles (Abstract) and that such compositions are preserved or stabilized by suspension in a liquid (Column 9, Example 2). The Roser reference discloses the use of perfluorohydrocarbons as the liquid component but does not teach the use of ether, amine or thioether-based fluorinated solvents as described in the general formula of instant Claim 1.

The Johnson reference teaches a composition comprising a solid particulate drug composition with a fluoropolyether that forms a stable suspension (Abstract). The Johnson reference also teaches that such compositions may comprise hydrofluoroethers (Column 2, lines 41 – 42 and 59 – 64).

Regarding instant Claim 2, the Roser reference discloses compositions comprising particles that contain sugar glass (Abstract, Claim 1).

Regarding instant Claim 3, the Roser reference discloses formulations in which additional components are added to the particles to provide a density in which the particles are stably dispersed (Column 7, lines 16 – 18; Claim 13).

Regarding instant Claim 4, the Roser reference discloses that the liquid may be blended with different components to achieve the desired density (Column 5, lines 49 – 56).

Regarding instant Claim 5, the Roser reference teaches formulations comprising a perfluorocarbon and an additional component of instant Claim 1, such as perfluorodecalin and sugar glass (Column 9, lines 20 – 22).

Regarding instant Claim 6, the Roser reference discloses a formulation comprising in which the bioactive agent is a vaccine (Column 5, lines 40 – 44; Claim 17).

Regarding instant Claims 7 – 9, drawn to a formulation in which the particles are prepared by different methods, the Roser reference disclose that the particles may be made by the conventional techniques of spray-drying, freeze-drying and milling (Column 5, lines 65 – 67; Column 6, lines 6 – 7; Example 5).

Regarding instant Claim 10, the Roser reference discloses a method in which a selection of fluorinated solvents are selected in order to provide the required density matching Column 9, lines 20 – 27).

Regarding instant Claim 11, as noted in the rejection of instant Claim 1, the Johnson reference teaches a composition comprising a solid particulate drug

composition in which the liquid may comprise hydrofluoroethers (Column 2, lines 41 – 42 and 59 – 64).

Thus, it would have been *prima facie* obvious to one skilled in the art, to expand upon the use of perfluorohydrocarbons, as previously taught by the Roser reference, and create compositions comprising more modified highly fluorinated liquid derivatives, such as fluorinated ethers related to those cited in instant Claim 1, to arrive at the claimed invention.

In addition to the teachings of Johnson, one would have been further motivated by the teachings of Owens regarding the greenhouse effect of PFCs, as cited in the prior art disclosed in the Roser reference, to seek alternative components to any PFC-based composition. In a review, Owens also notes the high global warming potential of PFCs and the need to develop alternatives. The specific selection of ether-based fluorinated compounds as a suitable liquid component of the claimed invention is further guided by the teachings of Owens who discloses hydrofluoroethers as potential alternatives to PFCs (Abstract, 3rd paragraph, Table 2). Furthermore, the Owens reference specifically discloses the HFEs 7100 and 7200 as well as the critical property of density, in Table 4.

Thus, it would have been *prima facie* obvious to one skilled in the art to combine the teachings of the Roser reference with the teachings provided by Owens and Johnson to incorporate HFEs as alternative liquid components to provide the stabilized formulations of the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 – 6 and 10 – 11 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1 – 4 , 13 and 16 – 18 of Roser in U.S. Patent 6,190,701, in view of Johnson in US patent 5,376,359.

Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons below:

As noted in the 103(a) rejections above, the prior art disclosed by Roser cited compositions comprising an active ingredient comprising a bioactive compound preserved in sugar glass particles suspended in a fluorinated solvent. The Roser reference discloses the use of perfluorohydrocarbons as the liquid component but does not teach the use of ether, amine or thioether-based fluorinated solvents as described in the general formula of instant Claim 1. The Johnson reference teaches a composition comprising a solid particulate drug composition with a fluoropolyether that forms a stable suspension (Abstract). The Johnson reference also teaches that such compositions may comprise hydrofluoroethers. Thus, it would have been *prima facie* obvious to one skilled in the art, to expand upon the use of perfluorohydrocarbons, as previously taught by the Roser reference, to examine more modified highly fluorinated liquid derivatives, such as fluorinated ethers related to those cited in instant Claim 1 to arrive at the claimed invention.

Conflicting Claims 1 – 4 disclose a composition cited in instant Claims 1 and 2. The conflicting claims do not teach the use of ether-based fluorinated solvents which, as noted above, is taught by the Johnson reference. Conflicting Claim 13 discloses the density matching formulation regarding the particles cited in instant Claim 3 while conflicting Claim 16 discloses the formulation regarding the composition of the liquid component. Conflicting Claim 17 discloses that the bioactive compound may be a vaccine, which is cited in instant Claim 6.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DENNIS HEYER whose telephone number is (571)270-7677. The examiner can normally be reached on Monday-Friday 8AM-5PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached on (571)272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DH

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